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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/935,124	08/21/2001	James B. Lorens	021044-000210US	8377

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TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER

HADDAD, MAHER M

ART UNIT PAPER NUMBER

1644

DATE MAILED: 02/25/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/935,124	LORENS ET AL.	
	Examiner	Art Unit	
	Maheer M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 December 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) 7-13, 17, 18 and 20-27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6, 14-16 and 19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>8</u> . | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

1. Claims 1-27 are pending.
2. Applicant's election with traverse of Group III, claims 1-6, 14-16 and 19 drawn to a method for identifying a compound that modulates angiogenesis in vitro, wherein the compound is a small organic molecule filed on 12/26/02, is acknowledged.

Applicant's traversal is on the grounds that (1) some claims were placed in different Groups, thus the rejection is improper and should be withdrawn, (2) Examiner may not reject a particular claim on the basis that it represent independent and distinct invention, (3) Examining claims of Groups 1-22, 23-25 and 26 together does not place an undue examination burden on the Examiner. This is not found persuasive because Examiner has not "rejected" any claim in the Office Action mailed on 8/13/02 (paper No.12). Further, the different methods of identifying and modulating angiogenesis differ with respect to ingredients, method steps, and endpoints; therefore, each method is patentably distinct and recognized divergent subject matter. Therefore those methods are distinct and independent, and searches of all groups would place an undue burden upon the examiner due to the distinct and divergent subject matter of each Group.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 7-13, 17-18 and 20-27 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.
4. Claims 1-6, 14-16 and 19 are under examination as they read on a method for identifying a compound that modulates angiogenesis in vitro, wherein the compound is a small organic molecule.
5. The following is a quotation of the second paragraph of 35 U.S.C. 112.
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
6. Claims 1-6, 14-16 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
 - A) The recitation of "hybridizes under stringent conditions" in claim 1, line 4 is ambiguous. Although the specification discloses on page 13 general parameters for calculating such conditions, it is unclear which conditions are actually claimed.

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It is suggested that Applicant amend the claims to recite a particular set of hybridization and wash conditions, such as those exemplified on page 13 of the specification, to overcome this rejection.

- B) The recitation of "ILKAP polypeptide" in claim 1, line 3 does not correspond to the recitation "the polypeptide encoded by a nucleic acid that hybridizes under stringent conditions to a nucleic acid encoding a polypeptide comprising an amino acid sequence of SEQ ID NO: 2", the translation of the complementary (antisense) sequence of the nucleic acid sequence encoding SEQ ID NO: 2 does not encode the ILKAP polypeptide.
- C) Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is: the resolution step, it unclear how to determine the inhibition. No proper controls are setup to compare the inhibition of angiogenesis.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-6, 14-16 and 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not reasonably provide enablement for an *in vitro* method for identifying a compound that inhibiting angiogenesis wherein the method comprises the steps of (i) contacting the compound with a ILKAP polypeptide, the polypeptide encoded by a nucleic acid that hybridizes under stringent conditions to a nucleic acid encoding a polypeptide comprising an amino acid sequence of SEQ ID NO: 2; and (ii) determining the functional effect of the compound upon the ILKAP polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546(BPAI 1986). They include the nature of the invention, the state of the art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

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The claims are broadly drawn to identifying a compound that modulate angiogenesis which effect the ligand binding to ILKAP polypeptide, the "polypeptide encoded by a nucleic acid that hybridizes under stringent conditions to a nucleic acid encoding a polypeptide comprising an amino acid sequence of SEQ ID NO:2".

The specification teaches (page 26, lines 3-31) that the assay for modulators of ILKAP protein and angiogenesis require the ILKAP protein of SEQ ID NO:2.

One cannot extrapolate the teachings of the specification to the scope of the claims because the method claims are drawn to the polypeptide that is encoded by a complementary (antisense) sequence of a nucleic acid encoding SEQ ID NO:2 which is not the ILKAP polypeptide of SEQ ID NO:2. The complementary sequence of the nucleic acid encoding SEQ ID NO: 2 has no open reading frame (ORF) for ILKAP polypeptide. The resultant polypeptides do not have the biological properties representative of what is being claimed, and applicant has not enabled any of these types of polypeptides because it has not been shown that these polypeptides are capable of functioning as that which is being disclosed.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, Burgess et al (J Cell Biol. 111:2129-2138, 1990) show that a conservative replacement of a single "lysine" residue at position 118 of acidic fibroblast growth factor by "glutamic acid" led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Similarly, Lazar et al. (Mol Cell Biol. 8:1247-1252, 1988) teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagines did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. Wen S *et al* (Proc Natl Acad Sci U S A. 98:4622-4627) demonstrate that a mutation in PTEN (G129E), a phosphatase with specificity for 3-phosphorylated inositol phospholipids, impaired the lipid phosphatase activity and its role in angiogenesis. These references demonstrate that event a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein.

The fact that two nucleic acid sequences will hybridize under moderate or stringent conditions does not in and of itself require that the two sequences share any functional activity. Thus the same observations apply to the recitation of "a nucleic acid that hybridizes under stringent hybridization conditions" with respect to "a nucleic acid encoding a polypeptide comprising an amino acid sequence of SEQ ID NO:2" language. Further, it was well known in the art at the time the invention was made that hybridization could occur between two sequence based upon short stretches of 100% identity. Thus a great deal of sequence variability *with respect to the full-length nucleic acid* is possible. In the absence of a clear recitation that the identity is over the full length of the nucleic acid encoding SEQ ID NO:2 the claim reads on subsequences. Thus as for the recitation of hybridization language in the absence of *a testable function* and limitations regarding both the *hybridization conditions* and the *sequence length over which the hybridization takes place*; does not allow the skilled artisan to make and use the

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hybridizing nucleic acids commensurate in scope with the instant claims without undue experimentation.

The term “comprising” in claim 1 is open-ended, it expand the polypeptide portions of SEQ ID NO: 2 to include additional non disclosed amino acids on the C-termini or N-Termini or both.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

9. Claims 1-6, 14-16 and 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is not in possession of any *in vitro* method for identifying a compound that inhibiting angiogenesis wherein the method comprises the steps of (i) contacting the compound with a ILKAP polypeptide, the polypeptide encoded by a nucleic acid that hybridizes under stringent conditions to a nucleic acid encoding a polypeptide comprising an amino acid sequence of SEQ ID NO: 2; and (ii) determining the functional effect of the compound upon the ILKAP polypeptide.

Applicant has disclosed only amino acid of SEQ ID NO: 2; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1 “Written Description” Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought,

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he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
February 24, 2003


CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600